

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

(51) International Patent Classification

A61K 31/19, 31/16

(11) International Publication Number:

WO 94/13280

A1

(43) International Publication Date:

23 June 1994 (23.06.94)

(21) International Application Number: PCT/US92/10452

(81) Designated States: AU, CA, JP, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

(22) International Filing Date: 4 December 1992 (04.12.92)

(71) Applicant (for all designated States except US): MAYOR  
PHARMACEUTICAL LABORATORIES, INC. [US/US];  
2401 South 24th Street, Phoenix, AZ 85034 (US).

Published

With international search report.

(72) Inventor; and

(75) Inventor/Applicant (for US only): DEIHL, Joseph, A.  
[US/US]; 4627 E. Foothill Drive, Paradise Valley, AZ  
85253 (US).(74) Agent: DRUMMOND, William, H.; 4590 MacArthur Boule-  
vard, Suite 500, Newport Beach, CA 92660 (US).

(54) Title: SPRAYABLE ANALGESIC COMPOSITION AND METHOD OF USE

(57) Abstract

A sprayable analgesic composition comprising an analgesic compound which is absorbed into the bloodstream through the buccal mucosa and a pharmacologically acceptable liquid carrier.

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgyzstan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LU	Luxembourg	TD	Chad
CS	Czechoslovakia	LV	Latvia	TG	Togo
CZ	Czech Republic	MC	Monaco	TJ	Tajikistan
DE	Germany	MD	Republic of Moldova	TT	Trinidad and Tobago
DK	Denmark	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	US	United States of America
FI	Finland	MN	Mongolia	UZ	Uzbekistan
FR	France			VN	Viet Nam
GA	Gabon				

SPRAYABLE ANALGESIC COMPOSITION AND METHOD OF USE

This invention relates to sprayable analgesic compositions.

10

In another respect, the invention pertains to methods of administering analgesic compounds.

15

According to another aspect, the invention pertains to compositions and methods for oral administration of analgesic compounds by absorption through the buccal mucosa.

20

Topical application of analgesic compositions, i.e., by application to and absorption through the skin, is known. For example, the composition for topical application of a salicylate emulsion foot spray is disclosed in a patent to Modderno (U.S. 2,975,097).

25

Sprayable topical analgesic anti-inflammatory compositions for treating skin rashes, etc. are disclosed in the Saitoh, et al. patent (U.S. 4,775,667).

30

Aerosol compositions for inhalation therapy, containing analgesics which are absorbed in the bronchioles and alveoli are disclosed in the patent to Porush, et al. (U.S. 2,868,691).

35

Liquid analgesics for oral administration are also known. For example, see the patent to Haas (U.S. 4,861,797) which discloses palatable liquid ibuprofen compositions.

To date, however, analgesic compounds have not been made available for administration by absorption through the buccal mucosa. It would be highly advantageous to provide such compositions in buccal absorption methods for administering analgesics, because such use and methods could be much more convenient for use by the general public, when it is not practical to use tabletted or swallowed liquid compositions. Moreover, compositions and methods for buccal mucosa administration of analgesics would be especially useful to persons who have impaired ability or aversion to swallowing tablets or liquid preparations.

Additionally, it would be advantageous to provide analgesic compositions and methods of administering analgesics which provide a desired physiological effect with the same or lower dosage compared to tabletted or liquid analgesic compositions.

I have now discovered liquid analgesic compositions and methods of administering analgesic compounds which are conveniently and inexpensively prepared, conveniently administered, and which may provide the desired physiological effect at a lower total dose than that obtained by use of prior tabletted or swallowed liquid compositions. My compositions and methods have been found particularly useful by persons who have a limited ability to use oral ingested tablets or liquids or have an aversion to such products. Further, it appears that a desired physiological result, i.e., alleviation of headaches can be obtained by administration of only approximately 1/20th of the dose normally recommended for tabletted analgesics such as acetaminophen.

Briefly, in accordance with my invention, I provide a sprayable analgesic composition comprising an analgesic compound which is capable of introduction into the bloodstream by absorption through the buccal mucosa in a pharmacologically acceptable liquid carrier. The viscosity of the composition is adjusted to permit spray application of the composition to the buccal mucosa. In a preferred embodiment, the analgesic compound is acetaminophen. In another embodiment, the analgesic compound is ibuprofen. In the preferred embodiment, the liquid carrier is an aqueous ethanol liquid.

According to another embodiment of the invention, the above-described composition is contained in a measured dose spray dispenser which delivers a physiologically effective quantity of the composition in one or more, preferably in from 1-5, measured doses.

According to yet another embodiment of the invention, I provide a method of administering an analgesic compound to a subject comprising dispersing a quantity of an analgesic compound which is absorbed by the buccal mucosa in a pharmacologically acceptable liquid carrier to form a sprayable liquid composition, introducing the liquid composition into a measured dose spray dispenser, and applying a physiologically effective quantity of said composition by spraying from said dispenser on the buccal mucosa.

As used herein, the term analgesic is intended to describe any of the several known analgesics, such as acetaminophen, aspirin, ibuprofen, naproxen and the like, some of which also exhibit anti-inflammatory and/or anti-pyretic physiological activity.

The compositions preferably also include, in addition to the analgesic and liquid carrier components, other optional ingredients such as surfactants, humectants, 5 preservatives, flavoring agents and other topical pharmaceutical adjuvants and excipients.

The compositions are prepared by art-recognized techniques which are typically used in the preparation of 10 similar sprayable compositions.

#### EXAMPLE I

15 The following example illustrates presently preferred practice of the invention and does not serve as a limitation on the scope of the invention which is limited only by the appended claims.

20 Having the following compositions:

	<u>Component</u>	<u>Parts by Weight</u>	<u>Description</u>
	SD alcohol	50	solvent
25	acetaminophen	12	analgesic
	distilled water	271	carrier
	sorbitol	.5	surfactant
	glycerine	50	humectant
	Sorbistat-K	.7	preservative
30	cyanocobalum	.02	Vitamin B <sub>12</sub>
	sucrose	220	flavor
	pyridoxine	3.6	Vitamin B <sub>6</sub>
	Tween 80	5	surfactant
	"Crest"	3	flavor
35	EDTA	.5	preservative
	fruit juice	2.5	flavor

5 The above-described composition is packaged in a measured dose spray dispenser containing enough of the composition to provide 240 spray doses containing 1 milligram acetaminophen per spray. (One spray equals 50 microliters.)

10 EXAMPLE II

Patients with common headaches are instructed to use the spray dispensers by administering two of the measured dose sprays into the mouth, on the inner cheeks and under the tongue, wait five minutes and then administer two more sprays in the same manner.

Simple headaches are relieved with one or two repetitions of the above procedure.

20 EXAMPLE III

Procedures of Examples I and II are repeated, except that the acetaminophen is replaced with ibuprofen. Similar results are obtained.

30 The sprayable compositions are, desirably, solutions of the active ingredients and other components. However, it is also contemplated that stable suspensions of the active ingredient and other components can be employed.



Having described my invention in such terms as to  
enable those skilled in the art to understand and practice  
it and having identified and disclosed presently preferred  
5 embodiments thereof, I claim:

1. A sprayable analgesic composition comprising:

5 (a) an analgesic compound which is introduced  
into the bloodstream by absorption through  
the buccal mucosa; and

10 (b) a pharmacologically acceptable liquid  
carrier for said analgesic compound;

15 the viscosity of said composition being adjusted to provide  
for spray application of the composition to the buccal  
mucosa.

2. The composition of claim 1 in which said analgesic compound is acetaminophen.

3. The composition of claim 1 in which said analgesic compound is ibuprofen.

4. The composition of claim 1 in which said liquid carrier is an aqueous alcoholic liquid.

5. The composition of claim 1 contained in a  
measured dose spray dispenser which delivers a  
physiologically effective quantity of said composition in  
5 from about 1-5 measured spray doses.

6. A method of administering an analgesic compound comprising:

5

(a) dispersing said analgesic compound in a pharmacologically acceptable liquid carrier to form a sprayable liquid composition;

10

(b) introducing said sprayable composition to a measured dose spray dispenser; and

15

(c) applying a physiologically effective quantity of said composition by spraying from said dispenser on the buccal mucosa.

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) A61K 31/19.31/16

US CL 514/570.629

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

STN: CAS online, APS

Search Terms: acetaminophen, ibuprofen, and analgesic in combination with spray, sprayable, and buccal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, A, 4,704,406 (STANISLAUS ET AL.) 03 November 1987, See entire document.	1,3-6
Y	US, A, 5,143,731 (VIEGAS ET AL.) 01 September 1992, See col. 10, line 32.	1,2,4-6

☐ Further documents are listed in the continuation of Box C.
 ☐ See patent family annex.

## \* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be part of particular relevance

\*E\* earlier document published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\*

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principles or theory underlying the invention

\*X\*

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\*

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

\*Z\*

document member of the same patent family

Date of the actual completion of the international search

13 MAY 1993

Date of mailing of the international search report

02 JUN 1993

 Name and mailing address of the ISA/US  
 Commissioner of Patents and Trademarks  
 Box PCT  
 Washington, D.C. 20231

Facsimile No. NOT APPLICABLE

Authorized officer

WILLIAM JARVIS

Telephone No. (703) 308-1235